and 60 ± 7.8%, respectively. The 1 and 5yr overall survival (OS) for pts with non-malignant disease was 82 ± 6.6%. The 5yr OS in children with PGF was 45.5 ± 15%. In conclusion, RI-AlloSCT is safe and well tolerated in children; RI-AlloSCT is associated with significantly lower NRM and high sustained donor chimerism. However, chemo-naïve children receiving UCB have a higher incidence of PGF and need alternative conditioning.

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UNRELATED UMBILICAL CORD BLOOD TRANSPLANTATION IS AN EFFECTIVE THERAPY FOR WISKOTT-ALDRICH SYNDROME

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Background: Patients with severe Wiskott-Aldrich Syndrome (WAS) characterized by absent WAS protein rarely survive beyond 20 years. Infections, hemorrhage and malignancy are leading causes of death. Allogeneic bone marrow transplant corrects immune function and thrombocytopenia and prolongs survival. However, many children lack an appropriate donor. This study investigated the feasibility of unrelated umbilical cord blood (UCB) as an alternative source of stem cells in WAS patients lacking HLA-matched bone marrow donors.

Methods: Fifteen children with severe WAS received 16 unrelated UCB transplants at Duke University from 2/1998 to 12/2007. All patients received myeloablative chemotherapy (busulfan, cyclophosphamide, ATG ± fludarabine). Patients were evaluated for engraftment, graft versus host disease (GvHD), survival and effects on the natural history of disease.

Results: UCB units matched at ≥4/6 HLA markers had a median precryopreservation total nucleated cell dose of 7.95×10^7 cells/kg. All patients engrafted with donor cells (one after a second UCB transplant). Median times to neutrophil (ANC > 500/uL) and platelet (>50k/L) engraftment were 21 (range 10–38) and 67 (range 46–139) days, respectively. One patient has mixed chimerism, all others maintained complete donor chimerism post-transplant. Four patients experienced grade II-IV acute GvHD and 11/12 evaluable patients experienced limited (n = 10) or extensive (n = 1) chronic GvHD. Six patients died post-transplant of gut GvHD with adenovirus, extensive chronic GvHD with EBV lymphoproliferative disorder, multisystem organ failure, and three of infection alone (Klebsiella, parainfluenza, adenovirus). Nine patients are surviving with a median follow-up of 89 months (range 9–127), an overall survival of 60%. Survivors have normal platelets, minimal eczema or other medical issues. All school-age children are attending school.

Conclusions: Unrelated UCB is a readily available source of stem cells for patients with WAS. UCB transplant corrects the immunodeficiency and thrombocytopenia caused by WAS and favorably impacts the natural history of disease. An increased incidence of limited chronic skin GvHD was noted compared to that reported in UCB transplant recipients with other diagnoses, perhaps related to pro-inflammatory state of the skin due to pre-transplant WAS-associated eczema. UCB transplantation should be considered for all patients with severe WAS lacking a matched adult or related bone marrow donor.

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SIGNIFICANCE OF HLA-B ANTIGEN MATCHING IN EVENT FREE SURVIVAL (EFS) IN PEDIATRIC UMBILICAL CORD BLOOD TRANSPLANTATION (CBT): EXPERIENCE FROM 124 SINGLE CBT AT CHILDREN'S MEMORIAL HOSPITAL (CMH), CHICAGO

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Objective: To evaluate the significance of HLA antigen matching/ mismatching in CBT outcomes in the pediatric patient.

Method: Between 1995- 2007, 124 single CBT were performed at CMH for treatment of malignancy (85) or non-malignancy (39). Diseases included ALL (39), AML (29), MDS (7), NBL (2), other malignancies (8), SCID (11), THAL (3), WISK (3), Osteopetrosis (4), AA (2), Fanconi's (2), other non-malignancies (14). Status at transplant for malignancies: CR1 (42%), CR2 (44%), CR ≥3 (7%) and PR (7%). Cord blood units were processed as described by Rubenstein *et al.* Recipients were 55 female, 69 male, median age at transplant 3.7 yrs (0.56 – 20.8), weight 20 kg (3- 73). 113 pts (91%) received myelo-ablative therapy of fTBI ± VP, Cy, TT (84), Bu, Cy ± VP (21) or TT, Cy ± FLUD (8) 11 pts (9%) received non-ablative regimen of VP, Cy, or FLUD ± Bu, Cy. GVHD prophylaxis was CSA + MTX + ATG . Prior to 2000, HLA matching for class was done by serologic typing. Later, high level molecular typing was done for HLA-DRB1. Degree of HLA matching was 6/6 (13), 5/6 (29), 4/6 (74), 3/6 (7). 5/6 HLA group: single mismatch on HLA-A (13), HLA-B (10), HLA-DRB1 (6). 4/6 HLA group: 2 mismatches, HLA-B (9) and DRB1 (1); other 64 pts had 1 mismatch on different antigens: A (43), B (51), DRB1 (34). 3/6 HLA group: 4 pts had 1 mismatch on each HLA antigen 3 patients had 2 mismatches on HLA-B + another mismatch. 30 patients (24%) died of TRM. 17 of 85 pts (20%) relapsed. 39% developed acute GVHD grade II/IV and 6.5% chronic GVHD. OS is 56% and EFS is 48% with median follow up of 763 days.

Results: Matching/mismatching at HLA-A, or HLA-DRB1 showed no statistical significance in TRM or EFS. Degree of HLA-B matching showed statistical significance in TRM and EFS (*p*-value 0.001). EFS, HLA-A: 1 match 56.5%; 2 matches 54.9%. EFS, HLA-B: 0 match 18.3%; 1 match 48.6%; 2 matches 72.3%. EFS, HLA-DRB1: 1 match 64%; 2 matches 51.1%. TRM, HLA-B: 11% (2 matches, n = 46), 31% (1 match, n = 65); 42% (0 match, n = 12). However, in analyzing the 4/6 HLA group alone, TRM for HLA-B antigen was 7% (2 matches), 25% (1 match) and 22% (0 match). In this group, the rate of relapse for pts with malignancy was 18% (2 matches), 5.7% (1 match) and 83.3% (0 match).

Conclusion: In pediatric CBT, TRM and Relapse increase with increasing HLA-B mismatch; and Event Free Survivals improve when HLA-B antigens are matched.

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TARGETING TO AN OPTIMAL AUC OF INTRAVENOUS BUSULFAN PREVENTS GRAFT FAILURE IN TRANSPLANTATION IN CHILDREN WITH NON-MALIGNANT DISEASES

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Background: Busulfan combined with therapeutic drug monitoring guided dosing is associated with higher event free survival (EFS) rates due to less graft-failure/relapses and lower toxicity in haematological stem cell transplantation (HSCT). In an earlier study, our group showed an optimal AUC between 74–82 mg*h/L with respect to event free survival (EFS) in a group of children with malignant and non-malignant indications. Non-malignant diseases, especially inborn error of metabolism (IEM) are known to be associated with high graft-failure rates. Therefore we analysed the influence of the "lower" limit of the (previously found) optimum of Busulfan AUC on graft-failure.

Methods: All children, transplanted between 2001–2008 in 2 Dutch pediatric transplant centers, receiving intravenous busulfan as part of a myeloablative regimen for non-malignant indications, were included. The association between an AUC below or above the lower limit of the optimum (74mg*h/L) and the main endpoints graft-failure and EFS and the toxicity endpoints treatment related mortality (TRM), acute-Graft-versus-Host Disease grade 2–4 (aGvHD) and Veno-occlusive Disease (VOD), were tested using uni- and multivariable Cox regression analysis.

Results: 70 patients were included (28 patients with IEM, 36 with immune defiencies (including Hemophagocytic Lympho-Histiocytosis) and 5 patients with bone marrow failures). Indications were equally distributed over the 2 groups. The median follow up time was 2.5 years (range 1–370 weeks). The AUC in the lower group ranged from 35.0–73.7 mg*h/L while those in the higher group ranged from 74.5 to 98.7 mg*h/L. EFS-rate in the <74mg*h/L group was negatively influenced by Graft-failure (18%, vs 0% in patients receiving >74mg*h/L, HR = 0.2, P = 0.016). EFS was 72% vs 82% in the <74 mg*h/L and >74 mg*h/L group, respectively. aGvHD grade 2–4 did occur more frequently in patients receiving a high exposure of busulfan (5% vs 19%: p = 0.2). No difference in TRM (P = 0.8) and VOD (P = 0.9) occurrence was noted as well.